

## Remarks

### I. Status of the Claims

As originally filed, the present application had a total of 18 claims. These have been cancelled herein and new claim 19 has been added.

### II. The Amendments

The specification has been amended to update information used in cross-referencing related applications and to correct a minor error with respect to a filing date. In addition, the abstract was amended to correct a grammatical error pointed out by the Examiner.

New claim 19 is fully supported by the claims originally in the application. It has been narrowed in order to comply with the restriction requirement imposed by the Examiner and now defines a much more homogeneous group of chemical compounds.

That amendments described above do not add new matter to the application, and their entry is therefore respectfully requested.

### III. Confirmation of Restriction Group Election

Applicants hereby confirm their election of restriction Group I. This is directed to compounds in which G is a nitrogen and A and B are carbocyclic rings. The claims in the non-elected restriction groups have been cancelled herein.

### IV. Response to Objection to Specification

On page 7 of the Office Action, the Examiner objects to the abstract based upon the allegation that the word "comprising" is grammatically incorrect and should, in fact, be "comprise." In response, Applicants have made the correction suggested by the Examiner and believe that the objection has therefore been overcome.

### V. Submission of Terminal Disclaimer

Applicants are submitting herewith a Terminal Disclaimer which disclaims the terminal portion of the term of any patent issuing in the present case which would extend

beyond the terms of either U.S. 6,130,622 or 6,680,321. This submission was made to overcome one of the double patenting rejections made by the Examiner.

## **The Rejections**

### **I. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph**

On pages 7 and 8 of the Office Action, the Examiner rejects claims under 35 U.S.C. § 112, second paragraph. Specific allegations are set forth in items 1-8. Below, Applicants respond to each allegation.

#### **A. Item 1**

In item 1, the Examiner argues that the phenyl rings shown as options for variable A are confusing because they show two bonds, one fixed and one floating. This allegedly makes it unclear how the rings are attached to the methylene carbon in the structure of Figure (I).

In response, Applicants have amended the structure shown in claim 19 so that there is no longer a floating bond. It is therefore respectfully submitted that any confusion regarding the attachment of the phenyl ring has been eliminated.

#### **B. Item 2**

In item 2, the Examiner argues that the word “substituent” following the words “ring of each A,” makes claim 1 confusing. Since this language is no longer present in amended claim 19, Applicants submit that this rejection has been obviated.

#### **C. Item 3**

In item 3, the Examiner indicates that claims are confusing because they refer to “C<sub>1</sub>” alkenyls when, in fact, such compounds require at least two carbons. In amended claim 19, the only alkenyl provided as an option is for variables R<sup>9</sup> and R<sup>10</sup> and, in this case, the claim refers to a “C<sub>2</sub>-C<sub>6</sub>” alkenyl. It is therefore respectfully submitted that claim 19 has been amended in a way that overcomes the rejection.

**D. Item 4**

The Examiner argues that the term “heteroaryl having from 5-10 atoms” is unclear because it includes structures that do not exist.

The only place where claim 19 refers to a heteroaryl is with reference to variable R<sup>1</sup>. Here, it specifies that a heteroaryl has five or six carbons. Since, heteroaryls with five or six members are clearly known, Applicants respectfully submit that the Examiner’s rejection has been overcome.

**E. Item 5**

In item 5, the Examiner points out that the term “naphthtyl” is misspelled. Since this term is no longer in claim 19, Applicants submit that the Examiner’s rejection has been obviated.

**F. Item 6**

In item 6, the Examiner objects to the use of the term “prodrugs” in claim 1. Since this term is no longer present in amended claim 19, Applicants submit that the Examiner’s rejection has been obviated.

**G. Item 7**

In item 7, the Examiner objects to a proviso that appeared in claim 2 based upon the argument that it is redundant. Since claim 2 has been eliminated, and claim 19 no longer contains a proviso, Applicants submit that the Examiner’s rejection has been obviated.

**H. Item 8**

In item 8, the Examiner rejects claim 3 as being indefinite because two variables, R<sup>7</sup> and R<sup>8</sup>, are not properly defined. Since claim 3 has been cancelled herein, and claim 19 defines all variables, Applicants submit that the Examiner’s rejection has been obviated.

**II. Rejection of Claims Under 35 U.S.C. § 101**

On page 8 of the Office Action, the Examiner rejects claims 6-11 because they are in a “use” format that is not permitted in the United States. These claims have been cancelled

and there are no use claims now pending. Therefore, Applicants submit that the Examiner's rejection has been overcome.

### **III. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph**

On pages 9 and 10 of the Office Action, the Examiner rejects claims under 35 U.S.C. § 112, first paragraph. The basis for the rejection is set forth in items 1-3. Below, Applicants respond to the arguments in each item.

#### **A. Item 1**

In item 1, the Examiner argues that the term "isomers" includes positional isomers that would not be fully enabled by the specification. In response, Applicants have indicated at the end of claim 19 that positional isomers are not included within the scope of the claim. Applicants therefore believe that the Examiner's rejection has been overcome.

#### **B. Item 2**

In item 2, the Examiner argues that the specification does not fully enable "prodrugs." Since this term has been eliminated from claim 19, Applicants submit that this rejection has been obviated.

#### **C. Item 3**

In item 3, the Examiner argues that claims are not fully enabled because they include a diverse array of compounds, and particularly, include heteroaryls as substituents on A and B rings, as well as for R variables.

Applicants submit that amended claim 19 defines a much more homogeneous group of compounds than original claim 1. Heteroaryls are still an option for variable R<sup>1</sup>, but they do not appear elsewhere in the claim and they are not an option as a substituent for A or B groups. In light of these changes, Applicants believe that claim 19 meets the enablement requirements of patentability and respectfully request that the Examiner's rejection be withdrawn.

**IV. Rejection of Claims Under 35 U.S.C. § 102 or 35 U.S.C. § 103**

On pages 11-13, the Examiner rejects claims either on novelty or obviousness grounds based upon several different references: Chang, *et al.* (WO 95/04051 and U.S. 5,681,830); Calderon, *et al.* (*J. Med. Chem.* 37:2125-2128 (1994)); and Bilsky, *et al.* (*J. Pharmacol. Exp. Ther.* 273:359-366 (1995)). In each case, the Examiner points to specific compounds in the references that are alleged to either anticipate claims or render them obvious.

In response, Applicants have examined each of the compounds cited by the Examiner and compared them with the compounds permitted by amended claim 19. It appears that all of the cited compounds fall outside the scope of the amended claim for at least two reasons: a) the cited compounds have piperazine rings with two methyl substituents, whereas Applicants' claims do not permit these substituents on piperazine rings; and (b) the cited compounds contain an allyl group at the position that appears to correspond to R<sup>1</sup> in formula (I) and this is not a permitted option. Based upon these structural differences, Applicants submit that the compounds in the cited references cannot anticipate claim 19. Moreover, the structural differences go beyond those that would generally be considered structurally obvious. It is therefore respectfully requested that the Examiner compare the cited compounds with amended claim 19 and reconsider the prior art rejections in light of Applicants' comments.

**V. First Double Patenting Rejection**

On pages 14 and 15 of the Office Action, the Examiner rejects claims under the doctrine of obviousness-type double patenting based upon U.S. 6,130,222 and 6,680,321. Both of these applications are relied upon for priority in the present case and Applicants are submitting a Terminal Disclaimer herewith that they believe should be sufficient to overcome this rejection.

**VI. Double Patenting Rejection Based Upon U.S. 6,696,447**

On pages 15 and 16 of the Office Action, the Examiner rejects claims under the doctrine of obviousness-type double patenting based upon U.S. 6,696,447. The '447 patent issued on February 24, 2004 and had an effective United States filing date (based upon an

international application) of March 30, 2001. It also claimed priority to an application filed in Sweden on April 4, 2000. As stated in the specification of '447, it does both disclose and claim certain compounds that fall within the range of compounds in WO 97/23466 (the published international application in the present case). However, the '447 patent also indicates that the compounds claimed therein were not specifically disclosed '466 (*i.e.*, they were only a part of a broader genus), and it refers to experimental results demonstrating surprising properties associated with the claimed compounds. In other words, the '447 patent is directed to a "selection invention."

Applicants respectfully submit that the '447 patent and the application upon which it is based is not prior art under any provision of United States patent law. There are two reasons for this. First, the present application is based upon (through two intermediate continuations) an international application that was filed on December 11, 1996, more than three years prior to the earliest filing for the application that eventually issued as '447. There is therefore no basis for an allegation of non-patentability under 35 U.S.C. §§ 102(e), (f) or (g). Second, the '447 application is directed to a distinct invention. Applicants could not claim the same compounds in the present case and it is well established that the patenting of a subset of compounds having surprising properties is proper in cases where they have previously been described or claimed only as part of a broader genus.

In light of the above considerations, Applicants respectfully submit that an obviousness-type double patenting rejection is inappropriate in the present case, and they therefore respectfully request that this rejection be withdrawn.

### **Conclusion**

In light of the amendments and discussion above, Applicants submit that all of the Examiner's rejections have been overcome. It is therefore respectfully requested that these rejections be withdrawn and that the claims presently pending in the application be allowed.

If, in the opinion of the Examiner, a phone call may help to expedite the prosecution of this application, the Examiner is invited to call Applicants' undersigned attorney at (202) 419-7013.

Respectfully submitted,

FITCH, EVEN, TABIN & FLANNERY

By Michael A. Sanzo

Michael A. Sanzo  
Reg. No. 36,912  
Attorney for Applicants

Date December 30, 2004  
1801 K Street, N.W., Suite 401L  
Washington, DC 20006-1201  
Telephone: (202) 419-7000